PHYS 597A, CMPSC 497E: Graphs and networks in systems biology

Spring 2009
T Th 9:45 - 11:00 am
105 Osmond Laboratory

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Office hours: Monday 1-3 pm

Many complex systems are difficult to describe and understand because they are composed of large numbers of elements interacting in a non-ordered way. A good example is cellular biology: diverse cellular components (genes, proteins, enzymes) participate in various reactions and regulatory interactions, forming a robust system. A very useful representation of complex systems is given by graphs (or networks), where we denote the components with nodes and their interactions by edges. The properties of these interaction graphs can then be analyzed by computational methods and this information can lead to important conclusions about the possible dynamical behaviors of the system.

This class will focus on four main questions:
(i) How do we determine or infer the interaction graphs underlying complex systems?
(ii) How can we characterize the organizational features of large-scale networks?
(iii) What are the mechanisms that determine the common topological features of a wide variety of networks?
(iv) To what extent does the organization of the interaction network underlying a complex system topology determine the dynamical behavior (e.g. steady state or oscillations) of the system?

Throughout the class the focus will be on biological networks and on the connections of network theory and computer science to systems biology. Systems biology topics will include inference of regulatory networks from gene expression data; analysis of protein interaction networks, metabolic networks and gene regulatory networks; continuous and discrete dynamical models of signal transduction and gene regulation.

This course will be concurrently offered as the special topics undergraduate course CMPS 497E and the special topics graduate course PHYS 597A. The lectures will be at an advanced undergraduate level. There will be differences in the assignments and grading of the undergraduate and graduate students.

Prerequisites

• MATH 017 (finite mathematics) or similar introduction to probabilities and combinatorics
• MATH 110 (techniques of calculus) or MATH 140B (calculus and biology) or similar introduction to calculus
• BIOL 011 or similar introductory biology
• BMB 211 or similar elementary biochemistry

These are not absolute prerequisites in the sense that the necessary background can be obtained by extra reading during the class. Supporting reading materials will be made available upon request.

Grades

CMPSC 497E: Grades will be based on homework assignments (60%) and a term paper (40%). Weekly homework will include exercises and critical reading assignments. There will be 10 homework assignments, graded on a 1-10 basis. The term paper will be a literature review on a topic of interest; a list of suggested topics will be provided. An outline of the paper will be due in March and a draft paper will be due in April. The final papers will be due on May 4, at 5 pm.

PHYS 597A: Grades will be based on homework assignments (50%) and a term paper (50%). Weekly homework will include exercises and critical reading assignments. There will be 10 homework assignments, graded on a 1-10 basis. Project topics will be selected from a list of suggestions or can be based on the research interests of participants. Work on terms projects will continue throughout the semester, with an abstract due in March and a draft paper due in April. Each participant will give a 10 minute project presentation during the last 3 classes. The final papers will be due on May 4, at 5 pm.

Each homework assignment for CMPSC 497E will be a reduced version of the homework assignment for PHYS 597A. The advanced (PHYS 597A only) question(s) will be clearly marked. Solution of these advanced questions by CMPSC 497E participants will be rewarded by extra credit.

Main topics covered

1. elements of graph theory: node degree, distances between nodes, clustering, node betweenness, subgraphs, directed graphs
2. graph algorithms and graph analysis/visualization software
3. analysis of cellular networks: gene regulatory networks, signal transduction networks, metabolic networks
4. random graph theory
5. network models and theory: lattices, small-world networks, scale-free networks, evolving networks
6. percolation and flow processes on networks
7. modeling the dynamics of reaction networks and of signal transduction networks
8. inference of gene regulatory networks from gene expression data
9. modeling the dynamics of gene regulatory networks

Important references (copies will be provided)

1. Réka Albert and Albert-László Barabási, Statistical mechanics of complex networks, Reviews of Modern Physics 74, 47-97 (2002).
2. C. Christensen, J. Thakar and R. Albert, Systems-level insights into cellular regulation: inferring, analyzing, and modeling intracellular networks, IET Systems Biology 1, 61-77 (2007).
3. John J. Tyson, Katherine C. Chen and Béla Novák, Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways in the cell, Current Opinion in Cell Biology 15, 221-231 (2003).

Reference books

1. Mark Newman, Albert-László Barabási, Duncan J. Watts (eds.), The Structure and Dynamics of Networks (2006).
2. Guido Caldarelli, Scale-Free Networks: Complex webs in nature and technology (2007).
3. Bernhard Palsson, Systems Biology: Properties of Reconstructed Networks (2006).
4. Uri Alon, An Introduction to Systems Biology: Design Principles of Biological Circuits (2006).
5. Björn Junker, Falk Shreiber (eds.), Analysis of biological networks (2008).
6. Francois Képès (ed.), Biological networks (2008).

Week	Date	Tuesday	Thursday
1	1/12	Introduction	Basic graph measures
2	1/19	Basic graph measures Homework 1 due	Graph algorithms
3	1/26	Topology of real networks Homework 2 due	Topology of biological networks
4	2/2	Random graph theory Homework 3 due	Random graph theory
5	2/9	Small-world and scale-free models Homework 4 due	Evolving networks
6	2/16	Biological network models Homework 5 due	Software for network analysis
7	2/23	Network resilience Homework 6 due	Resilience of biological networks
8	3/2	Spreading processes Homework 7 due	Epidemic models
9	3/9	No class	No class
10	3/16	Dynamics of cellular networks Abstract due	Reaction network dynamics
11	3/23	Dynamics of signal transduction Homework 8 due	Dynamics of signal transduction
12	3/30	Discrete dynamic simulations Homework 9 due	Random Boolean networks
13	4/6	Network inference Preliminary paper due	Gene regulation - continuous
14	4/13	Gene regulation - discrete Homework 10 due	Gene regulation - stochastic
15	4/20	Examples of current models	Examples of current models
16	4/27	Project presentations	Project presentations